

in the set as a product of the reagents or reaction conditions that the region was subjected to; and
e) repeating steps (b) through (d) until the desired library is obtained.

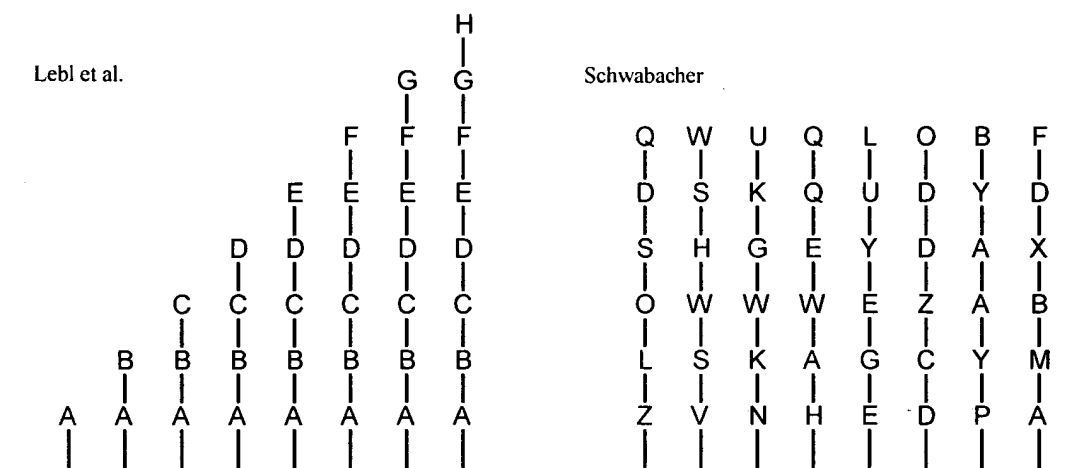
Please cancel claims ~~8-36~~, without prejudice.

Remarks

Claims 1-46 are pending in the application, and claims 8-36 have been withdrawn from further consideration by the examiner, 37 CFR §1.142(b), as being drawn to non-elected inventions. Claims 1-7 and 37-46 stand rejected. Non-elected claims 8-36 have been canceled. Claims 1-3 have been amended. No new matter is added to the specification by these changes. Applicant respectfully requests reexamination and reconsideration of the case, as amended. Each of the rejections levied in the Office Action is addressed individually below.

I. **Rejection under 35 U.S.C. §102(b), as being anticipated by EP 0 385 443.** Claims 1-7 and 37-38 stand rejected under 35 U.S.C. §102(b) as being anticipated by EP 0 385 443 by Lebl *et al.* Examiner takes the position that Lebl *et al.* describe at least two different chemical compounds attached to a linear support. However, the only way to have at least two different chemical compounds attached to the support in the system of Lebl *et al.* is if one stops the synthesis in the middle. In such a circumstance, all products on the support are necessarily related as intermediates on route to the synthesis of a single product. Lebl *et al.*, of course, acknowledges that they teach only a method of “obtaining some or all intermediates and eventually also the desired final product” (page 3, line 54). Thus, Lebl *et al.* do *not* teach a method of forming an array of at least two different chemical compounds wherein the chemical compounds are not intermediates leading to a single final product, as recited in amended claim 1. Support for this amendment to claim 1 can be found in Figure 2 as well as on page 11, lines 12-21, of the Specification as originally filed. Furthermore, one of skill in this art reading the present application would immediately appreciate that it is directed to arrays of diverse chemical

compounds which are not described in EP 0 385 443. The compounds of the arrays of the claimed invention are not intermediates on the way to a single final product. This difference between the arrays of the present invention and the band-like carriers of Lebl *et al.* stopped at a particular stage (claim 8 of EP 0 385 433) is illustrated below wherein, as a non-limiting example, the chemical compounds of the array are linear polymers:



Each compound of the Lebl band-link carriers is an intermediate along the synthetic route leading to the final product, ABCDEFGH, whereas the compounds of the arrays claimed by Schwabacher are each distinct final products themselves. Specific language to this effect has been added to independent claim 1 to make this point more clear.

Examiner has also stated that the reference reads on a support having one compound present at two different positions “since Lebl *et al.* teach a compound containing two glycine moieties” (page 7, lines 1-20 of EP 0 385 433). However, Applicant respectfully submits that the two glycine residues in Lebl *et al.* are incorporated into one polypeptide chain to yield methionine-enkephalin, TyrGlyGlyPheMet. The two glycine residues do not appear at two different positions along the array; both are incorporated into the same compound and therefore are at the same position in the array.

Therefore, EP 0 385 443 does not teach the invention recited in claim 1 of the present Application as amended herewith, and the Applicant respectfully submits that the rejection be removed.

Nor does Lebl *et al.* teach the invention recited in claim 2 or 3. Each of these claims recites a linear array produced by a process that necessarily creates a linear array in which compounds that are related to each other as products of identical reaction conditions are simultaneously generated at multiple positions along the array. In Lebl *et al.*, because the linear support is pulled through a series of reaction conditions, every compound on the support is produced in an identical series of reactions. Products resulting from a single set of reaction conditions are not separated from one another on the array by a specific spatial period, as recited in the present claims, but rather are arranged continuously along the support. Accordingly, Lebl *et al.* cannot anticipate the invention recited in independent claims 2 and 3.

II. Rejection under 35 U.S.C. §112, first paragraph, for lack of enablement. Claims 43-46 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. Examiner contends that although the specification is enabling for amino acids/peptides, it does not provide enablement for any “synthesis product”. Examiner maintains that undue experimentation would be required to prepare a claimed array with any synthesis product attached. Applicant respectfully disagrees with the Examiner’s view and points out that the specification provides significant guidance to those of ordinary skill in this art to prepare arrays containing any synthesis product without undue experimentation.

For example, the specification makes reference to a large number of publications describing known conditions for synthesizing small organic molecules on a solid phase/support (e.g., U.S. Patents 4,689,405; 5,445,934; 5,510,270; Thompson *et al.* *Chem. Rev.* 96:555-600, 1996; Bunin *et al.* *Proc. Natl. Acad. Sci. USA* 91:4708-4712, May 1994; Lam *et al.* *Chem. Rev.* 97:411-448, 1997; Liang *et al.* *Science* 274:1520, 1996; Nefzi *et al.* *Chem. Rev.* 97:449-472, 1997; Ohlmeyer *et al.* *Proc. Natl. Acad. Sci. USA* 90:10922-10926, 1993; cited in the Specification as filed at pages 1-3). One of ordinary skill in this art, having read the Specification, would have understood that any of the reaction conditions described in these, or related references, could be utilized in the practice of the presently claimed invention. Applicant acknowledges that the present specification exemplifies only peptide synthesis, but respectfully submits that the scope of enablement is not limited to the scope of exemplification.

As handed down by the Federal Circuit in *In re Wands* (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)), the “factors to be considered in determining whether a disclosure would require undue experimentation” include “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” With respect to each of these factors, (1) the quantity of experimentation necessary to practice the invention to the scope of the present claims would be quite small given the guidance in the specification and the knowledge in the art relating to solid phase synthesis of small organic molecules; (2) the amount of direction/guidance present in the disclosure is significant given the detailed description section of the specification and all the cited scientific references as described above; (3) the solid phase synthesis of peptides on a linear support is given as an example; (4) the nature of the invention is broad in scope given the implications for all types of combinatorial libraries whether they be oligonucleotide, peptide, or small molecule libraries that would be readily apparent to those of ordinary skill in the art; (5) the prior art is advanced with many known techniques and methods for synthesizing compounds on a solid support and in library form; (6) the relative skill of those in the art is high with most being at the Ph.D. level or beyond; (7) the art is reasonably predictable given the extensive research that has been done in this field over the last decade; and (8) the breadth of the claims covers linear arrays of any chemical compound that can be synthesized on a solid support including, but not limited to, peptides, polynucleotides, organic compounds, and small molecules, which is quite reasonable given the state of the art and the guidance provided by the specification. With little to no additional experimentation, one of skill in this art could prepare linear arrays of peptides, polynucleotides, small molecules, organic compounds, or other synthesis products; therefore, Applicant submits that the Specification is fully enabling and requests that the rejection be removed.

Also, allowing others to prepare arrays with chemical compounds other than peptides and avoid infringement would be against public policy. The inventor should be granted protection in proportion to his inventive contribution. Linear arrays of synthesis products provide a very powerful means of obtaining structure-function data on every member of a combinatorial library, regardless of its chemical structure. The present specification provides guidance sufficient to

allow those of ordinary skill to prepare linear arrays of a wide variety of chemical compounds. Limiting the present claims to peptide libraries would allow others to avoid literal infringement with a trivial change such as preparing a periodic, linear array of oligonucleotides or small molecules.

III. Rejection under 35 U.S.C. §112, second paragraph, as being indefinite. Claims 43-46 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner maintains that the term “synthesis product” is unclear, particularly when it is defined in later dependent claims as a “plurality of distinct chemical structures” or “single chemical structures”. Applicant submits that to one of ordinary skill in this art the term synthesis product would not be unclear.

However, to provide further clarification Applicant submits that the term synthesis product means any product of a synthesis reaction and has been used in claims 43-46 to mean any chemical compound including peptides, polynucleotides, small molecules, organic molecules, organometallic compounds, *etc.* These synthesis products are attached to the claimed array at distinct portions of the support. The dependent claims 44 and 46 further limit the synthesis products. For example, in claim 44, the synthesis product may be a plurality of distinct chemical structures. In other words, at any portion of the array, there may be a group of different chemical structures/synthesis products instead of just one. In claims 45 and 46, the synthesis products are limited to single chemical structures, meaning that all synthesis products at a portion of the support have the same chemical structure. Applicant submits that one of ordinary skill in this art would not find the Applicant’s use of the term synthesis product to be indefinite, and therefore, requests that the rejection be removed.

IV. Rejection under 35 U.S.C. §103, as being unpatentable over Lebl *et al.* (EP 0 385 443) in view of Lebl *et al.* (US 5,688,696). Claims 38-42 have been rejected under 35 U.S.C. §103(a), as being unpatentable over Lebl *et al.* (EP 0 385 443) in view of Lebl *et al.* (US 5,688,696). The teachings of Lebl *et al.* (EP 0 385 443) have been discussed above, and Applicant submits that the amended base claim 1, from which claims 38-42 depend, with the

limitation, "wherein the chemical compounds are not intermediates of a single final product," is not taught or suggested by EP 0 385 443. Furthermore, with respect to claims 38-42, Examiner admits that EP 0 385 443 lacks the teaching of duplicate compounds in different positions as set forth in these claims. Examiner then relies on U.S. Patent 5,688,696 to teach the making of arrays in duplicate so that a control can be used in the screening of the library. Applicant, however, submits that even in combination these references do not render obvious the claimed invention.

Examiner maintains that it was well known in the art at the time of the invention to make duplicate arrays of compounds and cites Lebl (US 5,688,696) as an example of making arrays in duplicate. Applicant submits that the present claims do *not* recite the making of *duplicate arrays* but rather the *duplication of certain compounds within one array*. Therefore, these references even when taken together do not teach the duplication of compounds within one array as claimed. In column 8, lines 9-42, Lebl suggests cutting in half the cotton pieces (line 8). The arrays of the present claims are continuous with "at least one compound present at at least two different positions on the support", and there is no teaching of cutting the array/support to form duplicates for screening. Even if one were to cut the arrays of Lebl in half, this would not lead to duplication of certain compounds within one array. One would just have two duplicate arrays, which is not the presently claimed invention.

Also, even if the U.S. Patent 5,688,696 did teach duplication, there is no suggestion or motivation to combine these two references. In particular the European patent teaches a continuous band with compounds attached to it, whereas the U.S. patent teaches cutting a cotton piece in half. One teaches a support which is continuous, and the other teaches dividing the support to form a duplicate. There is no motivation to combine these references, and Applicant submits that there is rather a teaching away from combining these references.

In light of the fundamental differences between what is claimed in the present application and the teachings of the cited references by Lebl as well as the lack of motivation to combine these references, Applicant requests that the Examiner remove the rejection.

In view of the forgoing arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, D.C. 20231 on April 6, 2001

